A NEWSLETTER WRITTEN BY ROSWELL PARK SCIENCE POLICY

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Note from the Chair:

I know that our news outlets and social media feeds are inundating us with constant information about COVID-19 – some useful and some confusing. With this constant stream of information and the impending opening up of our country, we as a group felt that it would be of great value to dive a little deeper into the many facets of COVID and provide some insights as young emerging scientists. We hope in this issue to provide you with both truthful and discerning pieces that will help to streamline this inundation of information.

As young scientists in this unprecedented time, we genuinely enjoyed discussing this issue and how best to present and provide this information to you. It is our hope that as you read through these articles the information is not just intellectually enlightening for you as scientists and clinicians- but also insightful and actionable for your family and friends as well.

Shivana Lightman

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Disclaimer: The goal of this newsletter is to provide information to researchers and clinicians regarding issues of science and policy. It is not our intention to express opinions – if any opinions are expressed, they are our own, and not on behalf of Roswell Park.

EPIDEMIOLOGY 101

JENNIFER MONGIOVI

Amidst all the articles, Tweets, and press conferences, you may have noticed data from epidemiologists are referenced as key sources of information. During an outbreak, information is gathered from clinical, laboratory, and epidemiologic sources to best estimate how the disease has and will affect a population.

So, what exactly does an epidemiologist do? Epidemiology, pronounced eh-puh-dee-mee-aa-luh-jee, is the study of the distribution and determinants of health-related states or events (including disease), and the application of this study to the control of diseases and other health problems (World Health Organization). Epidemiologists investigate the who, what, when, where, and why of a disease, which correlate with the stages of an outbreak investigation. Epidemiologists, scientists, and clinicians then work together to provide the statistics and evidence that are used to influence policy practices, such as mask use, occupancy restrictions, and lockdown approaches.

A lot of this information is available to the general public. With so much news being generated every hour, it can be a bit overwhelming trying to keep up and digest all this information. A few key phrases and a bit of 'Epidemiology 101' may help this material seem a bit more straightforward.

First, it's important to distinguish between the number of *incident* cases, which are new cases, and *prevalent* cases, which is the total number of cases. These measures are reported regarding a specific population of people, place or geographic location, and time. When being presented with information, it is important to keep in mind: What is the age, health status, and occupation of the population surveyed for this statistic? Where are these people located and is this a rural or urban area? When was this information gathered and over what time period?

Person, place, and time are also used to determine the level of disease. In epidemiologist terms, *endemic* is the baseline, or expected amount of disease within a given population in a specific place at a given time. When the amount of disease surpasses this level, often over a short period of time, it is considered an *epidemic*. The term *outbreak* is used in a similar way, but for a more specific area. When the disease

has spread across several countries and across continents, this becomes a *pandemic*.

To determine the severity of an outbreak, it is important to consider the classification of the cases being reported. *Confirmed* cases have been clinically tested and confirmed. A *suspected* or *probable* case has not yet been confirmed through testing but displays symptoms associated with the disease. Given the long turn around and limited availability of tests for COVID-19, suspected and probable cases should take precautions as if they are confirmed cases until proven otherwise to limit the spread of disease.

Epidemiologists also hope to limit the spread of disease through *contact tracing*, a strategy used to identify persons who may have come in contact with a confirmed case. Cases are interviewed and asked to recall where they had been or who they had been with during the period in which they were infectious. Public health officials then follow up with potential contacts so that they can take appropriate action, including monitoring their own health and minimizing additional contact with others.

The 5W's of descriptive epidemiology:

What = health issue of concern

Who = person

Where = place

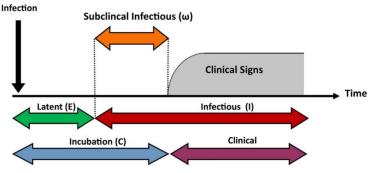
When = time

Why/How = causes, risk factor, modes of

transmission

What makes the COVID-19 pandemic especially complex is the variability in symptoms, incubation, and duration of infectivity. The period between when a person is exposed to the disease to when they show symptoms is called the *incubation period*. Right now, it is suspected that this is a period of two weeks for COVID-19. However, the *latent period* is the time between exposure to the disease and the ability to infect others. Because the incubation and latent period has varied widely from individual to individual, isolation, quarantine, and social distancing practices are incredibly important for minimizing the spread of this disease.

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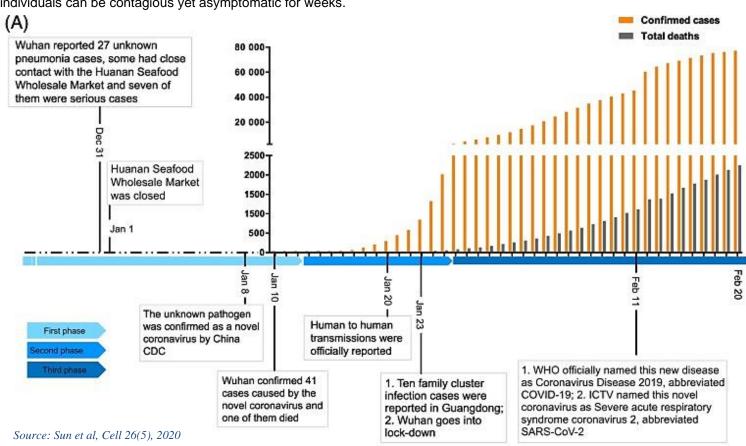


Artz et al. Scientific Reports, 9(2707), 2019.

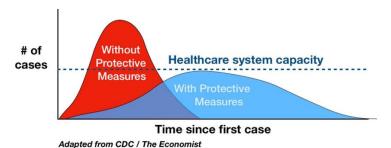
There are several social practices recommended to minimize the spread of disease and "flatten the curve," meaning to limit the number of people who are sick with the disease at a given time in order to allow hospitals, testing, schools, law enforcement, and other important organizations to be able to prepare and respond without completely exhausting resources. When someone is confirmed to have the disease, they should *isolate* or avoid contact with others who are not sick. *Quarantine* is a similar preventive measure that is practiced by seemingly individuals who may have come in contact with someone with the disease since they may be infected but not show symptoms. The current practice of social distancing is a way to limit contact with others since individuals can be contagious yet asymptomatic for weeks.

The availability of laboratory tests for COVID-19 also affects the ability of epidemiologists to accurately describe the true burden of this disease. This includes *infectivity*, or the proportion of individuals who have been exposed and become infected, and *pathogenicity*, or proportion of individuals who develop clinical symptoms (ex: fever, dry cough, and other symptoms thought to be associated with COVID-19). The extent of how contagious a disease is can be quantified using the *basic reproductive number* (R0) that provides an estimate of the number of subsequent cases as a result of exposure to a single case, assuming everyone in the given population is susceptible. Inability to confirm case status also affects estimates of *virulence*, also called the *case fatality rate*, which is the proportion of deaths among those with the disease.

The number of cases and/or deaths is divided by the population at risk, either at a single time point or over a given period, and then compared between populations. Therefore, it is crucial to review the specific person, place, and time used in each statistic or figure as these vary from source to source.



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Along with a few new vocabulary words, listed are some reliable sources of information for questions and concerns surrounding COVID-19:

Articles:

Misinformation during disease outbreaks can be difficult to address when there is some truth in it Elaine Nsoesie, PhD

Twitter:

Beth Linas, PhD, MHS - Infectious Disease & Digital Health Epidemiologist, MITRE

<u>Bill Miller, MD, PhD, MPH</u> - Infectious Disease Epidemiologist, The Ohio State University College of Public Health <u>Eleanor Murray, ScD, MSc, MPH</u> - Causal Inference Epidemiologist, Boston University School of Public Health

Podcasts:

Epidemiology Counts (Coronavirus, Follow-Up, Update) Society for Epidemiologic Research
Freakonomics Radio - Stephen Duber (Journalist) & Steven
Levitt (Professor of Economy)
The Readout LOUD - STAT
Science vs- Gimlet

Other.

Fighting COVID-19 with Epidemiology: A Johns Hopkins
Teach-Out - Free Online Course
Johns Hopkins Coronavirus Resource Center - Maps and trends

<u>How coronavirus charts can mislead us</u> - How to read the popular '-by country' chart



ABOUT THE AUTHOR

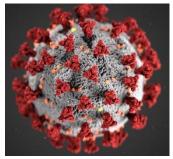
Credit: New York Times March 27, 2020

Jennifer Mongiovi is a PhD student in the department of Epidemiology and Environmental Health at the University at Buffalo. Prior to joining the program, she received a MS in Epidemiology from Columbia University. She is currently a T32 Cancer Epidemiology Trainee conducting her dissertation research on metabolic syndrome and ovarian cancer survival under the mentorship of Kirsten Moysich, PhD at Roswell Park.

THE NUTS AND BOLTS OF COVID-19

SHIVANA LIGHTMAN

The COVID-19 pandemic has brought about a slew of questions. What is a coronavirus? What is the severity of this disease? Is it like the flu, or worse? Can our immune systems fight this virus? Does a person who survives COVID-19 gain immunity? The question I hear most: is a vaccine being



developed, and when will it be ready?

The family called coronavirus

COVID-19 is a disease caused by the recently discovered virus SARS-Cov-2 and is part of the coronavirus family. Contrary to popular belief, it has no

connection to Mexico's finest beer. Corona is a Latin term meaning crown and was given to this family of viruses due to

SCIENCE IN FOCUS

the outer layer of protein spikes that cover them like a crown. These spikes (or coronas) are instrumental in the virus' ability to attach and infect target cells.

Viruses work by hijacking a cell's machinery to replicate as many viruses as possible, all before the body can raise the alarm and immune cells can fight off the infection. First identified in the mid-1960s, coronaviruses are part of a large family of viruses that typically cause mild to severe upperrespiratory tract illnesses. While there are hundreds of coronaviruses, most circulate among animals and do not infect humans. Four of the seven that can affect humans cause only mild to moderate illness, like the common cold. These are 229E, NL63, OC43, and HKU1. The remaining three are more serious and may lead to illness or death. These are SARS, MERS, and the above mentioned SARS-Cov-2. Aside from infecting the throat, airways, and lungs, these three can lead to severe complications such as pneumonia.

How does COVID-19 compare to the flu?

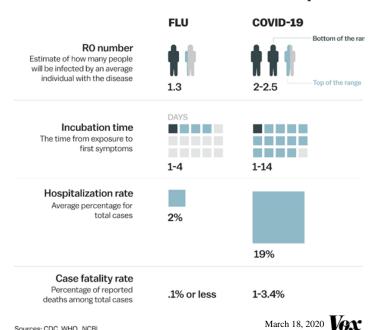
It is useful to note how infectious the three deadlier coronaviruses may be when compared to influenza. They have a significantly increased case fatality rate. The flu has a vaccine and people have had exposure to variants almost every year. This has allowed humans to gain some immunity to strains of influenza, which in turn provides a level of protection that is intrinsically missing with COVID-19.

What does this mean for immunity to COVID-19?

When a person is infected with a virus, they generally get an illness. When this happens, the immune system is alerted and starts producing antibodies. Antibodies are small proteins that "neutralize" the virus and rally a response from the rest of the immune system to fight off the virus. During this process, the immune system develops "memory," storing away information on said virus in case said person gets infected in the future. This memory allows the immune system to deploy rapidly, preventing someone from getting sick if they are exposed to the virus a second (or third, fourth, etc) time. There is a catch though...the robustness of protection varies depending on the virus. For example, the typical person has robust protection against the chicken pox but has less protection to the common cold.

The antibodies that are produced during an initial viral infection are unique to that virus and are an indicator that a person was previously infected. Scientists and doctors use

How seasonal flu and Covid-19 compare



this information to retrospectively analyze communities to determine who may have been infected with COVID-19. This is different than the diagnostic tests currently given to a sick person, which look for pieces of genetic material of the coronavirus (as opposed to antibodies). The antibody test may sound like a better way to test the population (as it may assess both those who currently have and formerly had the virus), but does have a few caveats:

1. Accuracy?

SARS-Cov-2 stems from a family of coronaviruses, some of which cause common colds. There is worry that some of these tests might not be specific enough and would pick up antibodies made for other coronaviruses.

2. It is unknown what level of antibodies provide immunity or how long this immunity lasts

Data shows that antibodies produced from infection with other coronaviruses, like SARS and MERS, persisted for at least a few years. This gives an indication that protection could last for at least this amount of time. Yet, as this pandemic is only a few months old, we cannot know for certain if this will be the



Epidemiological Comparison of Respiratory Viral Infections

Disease	Flu	COVID-19	SARS	MERS
Disease Causing Pathogen	Influenza virus	SARS-CoV-2	SARS-CoV	MERS-CoV
R ₀ Basic Reproductive Number	1.3	2.0 - 2.5 *	3	0.3 - 0.8
CFR Case Fatality Rate	0.05 - 0.1%	~3.4% *	9.6 - 11%	34.4%
Incubation Time	1 - 4 days	4 - 14 days *	2 - 7 days	6 days
Hospitalization Rate	2%	~19% *	Most cases	Most cases
Community Attack Rate	10 - 20%	30 - 40% *	10 - 60%	4 - 13%

Source: Epidemiological comparison of respiratory viral infections (Dr. Akiko Iwasaki, Yale University)

case. It is also unclear at this time what level of antibodies a person needs to be protected from reinfection with COVID-19.

3. What can these antibody tests tell us?

Using an antibody test can provide a broader idea of how widely the virus has spread in a population. In NY, it has been estimated that ~20% of NYC and ~14% statewide have antibodies to COVID-19. However, as tests are being refined, these numbers may change to reveal a more complete picture.

These low numbers of antibodies can tell us an obvious factnot enough of us are protected. We want people to have
Herd Immunity. This is a concept in which a population has
enough people immune to a disease that transmission, and
thus infectivity, is severely limited in that group. Herd
Immunity can take place in two ways: natural infection (and
antibody creation) or vaccination (also antibody creation).
For Herd Immunity to be effective, 70%-95% of the
population must be immune. As we do not have a vaccine for
COVID-19, the only current way for Herd Immunity to kick in
is for more people to get infected. For obvious reasons,
infecting the population with a deadly disease to create
protection for said deadly disease is not a popular choice.

Vaccination: the most viable option for our future

There are currently 115 vaccine candidates spanning the globe. Of these, 37 are unconfirmed (in development status in a lab setting) and 78 are confirmed (in exploratory, preclinical stages, or beyond). 56 of the 78 are being developed by private industry developers. The remaining 22 are being researched by academics in the public sector and non-profit organizations. Most of these developments are occurring in North America (46%), with 18% in China, 18% in rest of Asia and Australia, and 18% in Europe.

What many are calling the most promising vaccine candidate to date has come out of Oxford University's Jenner Institute. It is called ChAdOx1 nCoV-19. Previous trials using similar inoculations demonstrate that this vaccine is harmless to humans (author's translation: the 'backbone' that this vaccine is based on is not dangerous to humans, therefore making it a viable candidate as a vaccine). Because of this, it been fast tracked and should be tested in more than 6,000 people by the end of May. If this works, researchers hope that with emergency approval the first million or so doses could be available as early as September. Vaccines are how modern medicine has been able to go from just treating deadly illnesses to preventing them from occurring in the first place. Thus, the development of a vaccine would change what is our current approach of treating the disease

(whether this be through use of ventilators or drugs like remdesivir) to preventing illness and further outbreaks.

Our future living with COVID-19

As we approach summer, many are predicting (or hoping) that this pandemic will wane in the same manner as influenza. Evidence of milder coronaviruses shows that they often subside in warmer months. A recent MIT report states that most COVID-19 cases seem to spread in areas with lower temperatures and that regions with temperatures higher than 64.4 degrees Fahrenheit account for less than 6% of global cases so far. However, this is in direct contrast to countries that currently have "summer climates," like Australia and Iran. Both countries are experiencing a rapid spread of COVID-19. This is, unfortunately, casting doubt on how "seasonal" this virus may be.

In either event most pandemics experience waves. Health experts anticipate a second wave occurring in the Fall. Why? As time continues, restrictions for social distancing measures will inevitably ease. These measures may unfortunately cause a surge in the spread of the virus. As we move toward this possibility, health officials are proposing three steps to decrease the likelihood of this happening:

- Require everyone to wear masks: This will substantially reduce transmission of the virus as people start to venture back out into their communities and increased interaction takes place.
- 2. **Bring testing to the people:** We must quickly find those infected and stop onward spreading through testing, contact tracing, isolation, and quarantine.
- Prepare for COVID-19 rebounds: Until we have a vaccine another surge is likely. Hospitals and our healthcare system should take account and prepare for another wave in the near future.

These are all part of a concept akin to the layers of Swiss Cheese (as stated by Dr. Rajeev Venkayya). Like the layers of Swiss cheese, each imperfect barrier when layered together allow for gaps to be covered and viral transmission to be slowed.

TABLE 1 | CLINICAL-PHASE VACCINE CANDIDATES FOR COVID-19

Candidate	Vaccine characteristics	Lead developer	Status
mRNA- 1273	LNP-encapsulated mRNA vaccine encoding S protein	Moderna	Phase I (NCT04283461)
Ad5-nCoV	Adenovirus type 5 vector that expresses S protein	CanSino Biologicals	Phase I (NCT04313127)
INO-4800	DNA plasmid encoding S protein delivered by electroporation	Inovio Pharmaceuticals	Phase I (NCT04336410)
LV- SMENP- DC	DCs modified with lentiviral vector expressing synthetic minigene based on domains of selected viral proteins; administered with antigen-specific CTLs	Shenzhen Geno-Immune Medical Institute	Phase I (NCT04276896)
Pathogen- specific aAPC	aAPCs modified with lentiviral vector expressing synthetic minigene based on domains of selected viral proteins	Shenzhen Geno-Immune Medical Institute	Phase I (NCT04299724)

aAPC, artificial antigen-presenting cell; CTL, cytotoxic T lymphocyte; DC, dendritic cell; LNP, lipid nanoparticle; S protein, SARS-CoV-2 spike protein. Source: ClinicalTrials.gov website; WHO.

Source: Nature Reviews, Volume 19(5), May 2020.

About the Author:



Shivana Lightman is one of the founders and current Chair of our policy group. Her work, in the lab of Kelvin Lee, focuses primarily on understanding the key molecular mechanisms responsible for durable humoral immunity and survival of long lived plasma cells. Shivana's interests include the science of food and cooking, intersection of nutrition and the immune system, economics

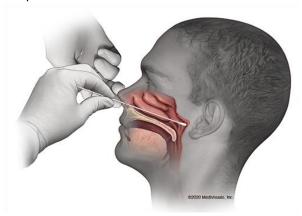
of science and, most of all spending time with her rambunctious puppy Theia.

TESTING CHALLENGES IN THE U.S.

JOSEPH INIGO

In the wake of the COVID-19 pandemic caused by SARS-CoV-2, proper testing has been paramount to understanding the spread of the disease. Tests which prove to be reliable continue to guide officials on how to combat the coronavirus. However, the last few months have been fraught with unexpected challenges in accurately testing for COVID-19.

Once China published the genome of SARS-CoV-2 in early January, researchers in Germany used this information to develop the first diagnostic test for COVID-19. This method utilizes reverse transcription polymerase chain reaction (RT-PCR) to detect distinct genetic components of SARS-CoV-2. The World Health Organization (WHO) adopted this protocol, but not all countries followed suit. For example, as per standard procedure during an outbreak, the US Centers for Disease Control and Prevention (CDC) developed their own test. This version also applies RT-PCR but targets different viral components of SARS-CoV-2.



Source: https://health.ucdavis.edu/coronavirus/coronavirus-testing.html

In a massive setback to the coronavirus response, early CDC test kits encountered performance issues. The Food and Drug Administration (FDA) determined that materials in the test kits were contaminated with the virus. The CDC had violated their own protocols by assembling these tests in laboratories housing coronavirus material instead of producing them in a separate manufacturing facility. Having taken over a month to resolve this issue and faced with

growing criticism, the FDA expanded the Emergency Use Authorization (EUA) policy at the end of February. This allowed the development and use of test kits by laboratories outside of the CDC, prior to a full FDA review and approval. As of May, approximately 55 RT-PCR based test kits have been fast-tracked through EUA, each targeting varying components of SARS-CoV-2.

As companies began supplying EUA-approved test kits, many proceeded to offer them for at-home use. The FDA clarified that the EUA policy does not automatically allow athome use due to concerns of improper sample collection in the absence of a healthcare professional. Recently, LabCorp demonstrated that their kits allow efficient sample collection without supervision and received authorization to deploy the first at-home test kit in the US.

The next step in tracking COVID-19 involves serology-based testing—screening the blood for specific antibodies produced to combat the coronavirus—to identify cases of COVID-19 which have ceased but were undiagnosed. While multiple serologic tests have been cleared for use through the EUA, caution is advised in interpreting the results. It can take the immune system days to produce antibodies after an infection and so, this test is unable to identify those who are in the early stages of the disease. Additionally, some patients in China confirmed for COVID-19 have been reported to produce low amounts of antibodies.

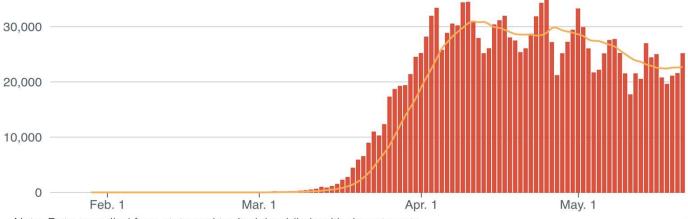
Meanwhile, the need for quicker testing has prompted the development of rapid diagnostic testing (RDT). Unlike standard practices, RDT requires only minutes to test patients and can be processed in a clinical setting. RT-PCR based rapid tests using portable devices from the likes of Abbott Labs and Cepheid have received EUA authorization. However, RDT is unlikely to replace laboratory testing due to the fewer number of samples which can be processed each day.

Communication issues continue to hinder testing. Clinicians must contact laboratories to assess if they have the capacity to receive samples. Errors have led to laboratories receiving more samples than they can manage or remaining idle and awaiting samples for processing. Yet, even in the best circumstances, samples might still be shipped to facilities hundreds of miles away.

US Daily COVID-19 New Cases

Numbers reported by state authorities as of May 21, 4pm ET

7 day rolling average



Note: Data compiled from state and territorial public health departments

Source: The COVID Tracking Project

Concerns remain over the sensitivity and specificity of COVID-19 tests, the ability to identify those with the disease (true positive) and those without the disease (true negative). Preliminary studies indicate that RT-PCR tests may provide a false negative 30% of the time, meaning that 30% of patients with COVID-19 are incorrectly identified as virus-free. This can be exacerbated if nasal swabs are not inserted far enough into the nose and throat to collect samples. Reports of recovered patients again testing positive for COVID-19 may be the result of previous false negatives or the detection of viral particles remaining in the system after the illness has passed. Nonetheless, ongoing evaluation of current test kits is imperative.

As we proceed, officials require a better picture of the extent to which COVID-19 has spread to begin reopening certain sections of the US. In addition to RT-PCR testing, the US has begun conducting serosurveys, random serological testing of the population to estimate the spread of the virus. Recent numbers show that nationally, about 17.5% of the people tested so far have been positive for COVID-19. This indicates that there is still a significant amount of the population who have the virus but have not been tested. Experts recommend expanded testing to detect regional decline in new cases and to identify smaller outbreaks before they become larger threats.

<u>Current guidelines for COVID-19 testing:</u> A shortage of test kits initially limited testing to patients who displayed

symptoms and recently traveled to China or contacted a person confirmed to have COVID-19. By early March, the CDC began allowing clinicians to recommend and conduct tests in order of priority: (1) hospitalized patients and healthcare workers, (2) elders in long-term care facilities, and (3) individuals with mild symptoms.

The COVID Tracking Project: An ongoing volunteer effort that compiles the cases of COVID-19 from public health authorities in the US each day. The amount of confirmed cases and total number of tests performed, by US state or territory, are presented. This tracker is currently in use by researchers and news organizations. https://covidtracking.com/.

About the Author:



Joseph R. Inigo is a doctoral candidate in the department of Pharmacology and Therapeutics in the lab of Dhyan Chandra, PhD. He currently focuses on prostate cancer and studies the role of the mitochondrial unfolded protein response in maintaining mitochondrial integrity to promote cancer growth and survival.

THE CASE OF COVID IN DEVELOPING NATIONS

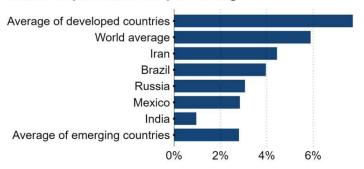
SHRUTI DIGHE

As stated by the World Health Organization (WHO), "the future of this pandemic depends on how densely populated countries contain this virus." What happens when travel and trade resume? Will these countries be responsible for new waves of cases worldwide? Will this be an unending cycle until a cure or vaccine is developed? The fear amongst the scientific community is legitimate as answers to these questions remain unknown. This virus does not discriminate regarding infections, a country's preparedness, resources, and response, or how their vulnerable populations tide through this evolving crisis. Populations of several hundred in nations like Africa, Asia and Latin America are growing twice as fast as that of the developed world. It is estimated that nearly four-fifths of the world's population resides in 'developing' and 'in transition' economies.

New COVID-19 cases Developed countries Emerging countries 60,000 40,000 20,000 Jan Feb Mar Mar Apr May Source: World Health Organization

A prime example of this is India. The World Bank estimates the current Indian population to be approximately 1.34 billion, over five times that of the United States. However, the Indian GDP is only ~\$3.2 trillion, compared to the \$19.4 trillion of the U.S. Thus, even under normal circumstances, developing countries are stretched thin, struggling with poverty, hunger, overcrowding, lack of healthcare resources and extreme socio-economic disparity. Pandemics such as COVID-19 pose additional challenges to meet basic needs for existence, all while trying to combat the mayhem that comes along with novel outbreaks.

Health expenditure as percentage of GDP



Source: World Health Organization

Nationwide lockdowns may seem extreme. However, given the highly contagious nature of this disease, it may be justified in densely populated countries. Reports in the Indian media suggest that suspension of all domestic and foreign travel may have been effective in slowing down the community spread of this virus. India has approximately 1 doctor per 1500 citizens in urban populations, 1 physician per 10,000 in rural areas, and 2.3 intensive care beds per 100,000 people. This is compared to 3.6 in China and 35 in the U.S. With an inadequate health care infrastructure to begin with, expansion of hospital capacity (a viable option for the developed world) seems like an impossible proposition for developing countries to combat the sudden surge of cases. It is nearly impossible for smaller economies to meet the demands for protective masks, gowns, hospital beds and life-saving equipment such as ventilators, without aid from global humanitarian organizations like the WHO and UN.

In Sierra Leone, Guinea, and Liberia, deaths of over 1,000 nurses, doctors and other health care professionals were reported, mainly due to a lack of personal protective gear and widespread testing. This quickly strained their already weak healthcare systems. Similarly, BBC news reported that with barely 60 ventilators for 11 million people, Haiti, the most vulnerable nation in the Americas, might never be able to recover from this pandemic. Not only are very few Haitian doctors trained to operate ventilators, but electricity required to run this equipment is very unreliable. Approximately 60% of the Haitian population who live below the poverty line continue to go about their usual business to put food on the table. The current case numbers seem low, perhaps due to inadequate testing, but very soon countries like Haiti may become hotspots. Physician and renowned global health expert, Dr. Paul Farmer, who has dealt with the AIDS, Ebola, cholera, and tuberculosis epidemics across Africa, Latin America, and the Caribbean, said "Increasing access to free and convenient testing is key. This is how transmission

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chains are identified and broken effectively". He also shed light on the fact that though there is assigned aid for poor economies such as the 'pandemic emergency fund' through the World Bank, it is extremely difficult to tap into such funding. His organization, the Partners in Health, has had to rely on private philanthropy to obtain basic medical supplies.

In addition, the economic fallout that developing countries are facing from such nationwide lockdowns and closure of all non-essential businesses will cause irreparable damage. Nations like Syria, Sudan, Myanmar among others, are struggling with problems related to their refugee camps, where thousands are crammed in small settlements. Ensuring social distancing to prevent COVID-19 outbreaks in such make-shift overcrowded dwelling is nearly impossible. Furthermore, supply chains for relief organizations have been disrupted due to diminishing humanitarian aid, travel, and transport restrictions. Reports suggest that there is already a growing shortage of food, medicine, and basic sanitation products in Syrian refugee camps. Furthermore, India had to deal with a unique problem related to their migrant workers living in big cities who depend on daily wages for sustenance. Several thousands of them set out on foot, willing to walk hundreds of miles to reach their homes and families in rural locations, in the hope of sustaining, versus perishing in unhygienic crowded locations without food or money due to closure of businesses. This further increases the risk of mass outbreaks with such population movements.



It appears some nations like India have had a successful start in preventing the exponential spread that was originally predicted to occur among their population. The nation's apical research institute, the Indian Council of Medical Research, reported that as of March 31st there were ~800 cases in the entire country with no evidence of community spread. This number has currently risen to nearly 25,000 cases, which still seems low given the country's sociodemographic structure, as compared to the 1.53 million cases in the U.S (as of 5/18/2020). The ongoing debate

remains regarding the **'true case numbers'** due to inadequate testing, quality of locally developed tests, and potential false negatives. The high population density in developing nations also makes it challenging to track and report accurate disease outcomes, trace, and confine contacts of COVID positive individuals, and ensure quarantine.

The COVID-19 pandemic has made it clear that despite socio-economic differences, every country in the world is facing a common threat. Now more than ever, it is imperative that countries share resources and scientific knowledge to not only ensure an effective end to this crisis, but also prevent future disease outbreaks.

larger than in any advanced economy.

For many developing countries, the crisis may barely have begun, and the human toll of a major COVID-19 outbreak would be orders of magnitude

Mohamed A. El-Erian
Chief Economic Adviser, Allianz

About the Author:



Shruti Dighe works with Matthew Buas PhD, in the Department of Cancer Prevention and Control. She is currently studying the genetic susceptibility and survival among esophageal cancer patients. She received her medical degree in India and a masters in Epidemiology at UB. She was also the co-chair of the First year student mentoring committee 2019-2020 and an active member of the Delta Omega Honor Society for Public Health.

NO COUNTRY FOR UNINFECTED MEN:

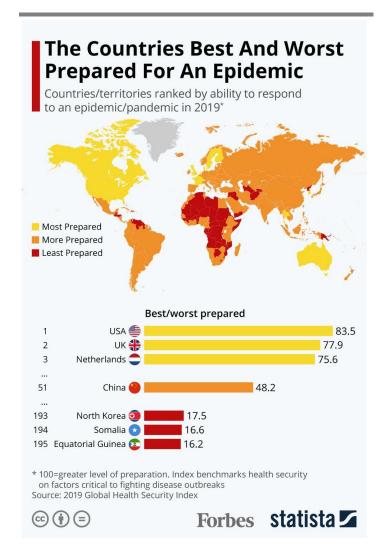
SHIN LA SHU

The societal response to COVID-19 is uncannily like the 2007 film by the Cohen brothers, "no country for old men". The heroes (medical staff) lose their lives and the villain (coronavirus) gets away every time, and how it ends is narrated by people who are the least involved in the action (people choosing to stay at home).

As of the end of April, worldwide infections have exceeded 3 million and accounted for at least 200,000 deaths worldwide in a matter of four months. Depending on where you live, the mortality rate after infection ranges between 0.08% to 15.49%. In a hypothetical playout of a pandemic, one can logically assume that high infection and high death rates would be associated with developing nations (struggling to supply basic resources and hygiene facilities to its people), whereas developed nations would be much more resilient to a pandemic outbreak. We now know that such a simplified model catastrophically fails to explain the magnitude of infection sweeping across many developed countries. This article will focus on key public policies that developed nations have rolled out to counter specific weak points in their unique cultures and fight the COVID-19 outbreak.

Armed to the teeth: Singapore's COVID-19 response Southeast Asia

For some countries, the term "weaponized" would be more apt to describe the execution of certain public policies enacted for the COVID-19 pandemic. Singapore would fit such a description in their enforcement of public policy. At the initial outbreak, Singapore was one of the few countries, beginning with patient zero, that enforced contact tracing and quarantine. The implemented policies included mandatory quarantine observation by law, with consequences including fines, confiscation of one's passport and even jail terms. For example, a man who escaped quarantine orders to visit a restaurant to eat "Bak Kut Teh" (pork bone soup, a Singapore delicacy) was jailed for three weeks. Such policies worked very well initially, and Singapore had reported only 3 deaths in the first three months since its first COVID-19 case. Singapore's economic activity was near normalcy until late March, and its public policies were praised by the World



Health Organization (WHO) as the "gold standard". But despite their best efforts, the return of foreign workers in April, brought about severe outbreaks in construction worker dormitories, leading to thousands of positive cases a day. This has led to implementation of a lockdown policy informally known as the "Circuit Breaker Policy" This forbids commuting and activities that are non-essential, including dining at restaurants. Social distancing is enforced through fines and all non-essential activities, including commercial activities, have been shuttered until further notice.

Lockdowns work: New Zealand's COVID-19 response - Australasia

New Zealand was fortunate that patient zero was detected early in February, a full month after the initial outbreak of

cases in the United States. The country's Prime Minister, Jacinda Ardern, knew that New Zealand would be easily overwhelmed as most medical supplies were imported. She quickly contacted nearby countries (including Singapore) for advice on public policies and rallied the country to pursue a strategy of "elimination" (i.e. complete lockdown) rather than mitigation or suppression. The approach was simple but highly effective. She brought New Zealand to a complete uncompromising lockdown on March 23rd, when New Zealand had just surpassed 100 cases. She is guoted as saying "we have 102 cases, so did Italy once". All airports and gathering places were closed and events that involved gathering were cancelled. The New Zealand government website also has a link to report any breach in lockdown practices to the authorities directly, bringing "neighborhood watch" style reporting network to cover an entire nation. Unlike the rest of the world, New Zealand declared its victory against the COVID-19 pandemic on April 28th and has largely left businesses to decide whether they will open, but to do so safely- for now.

When your leader is a scientist: Germany's COVID-19 response - Western Europe

Angela Merkel, Ph.D., is the Chancellor of Germany and the de facto leader of her nation since 2005. When the outbreak reached Germany, she already had several policies in place to deal with the pandemic. Amongst the most notable of them was the creation of a detection kit for COVID-19 far earlier than any other country. With generous and sustained support into virus research from Dr. Merkel and the government, Germany created the world's first diagnostic test for SARS-CoV-2 in mid-January (a week after China released the virus genome). The manufacturing process was rapidly shared with the world. Early detection was done at a massive scale (200,000 tests per week), and this has indirectly helped to keep death rates comparatively low (1.5%) despite having more than 100,000 positive cases.

The government website has also made available an easy-to-print one-page pamphlet on the "Current Information on the Coronavirus". This pamphlet informs everyone on a three-pronged approach against the outbreak, namely to "Protect!", "Recognize!" and "Act!". She has repetitively emphasized that "our own behavior is currently our most effective measure". Starting May 6th Germany will no longer enforce social distancing, and will implement a point of contact for local health authorities to directly contact the Koch Institute (a leading research institute in Germany) to "precisely reconstruct the chains of infection" as the surest

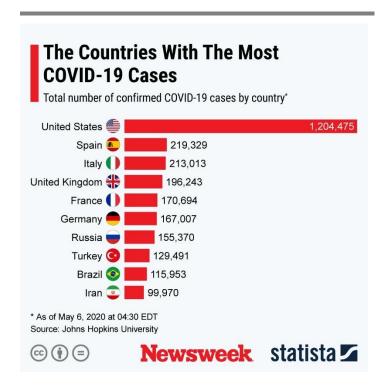
way in slowing the spread of the virus. Dr. Merkel has warned that a second wave of outbreak may occur if reopening of the country is not handled properly.

Contact tracing works: South Korea's COVID-19 response - *East Asia*

South Korea's response is known for its technology-based, informatics-heavy response. A COVID-19 response agency was set up, allowing nearly all contact tracing efforts (age, location, date and time of visited places before quarantine) to be made public and updated immediately. To ensure people stayed in their homes during the 14-day mandatory quarantine period after returning from overseas travel, contact-tracing apps were installed into smartphones to alert the authorities when a person left his or her home. A CNN reporter published his experience of a "drive-thru coronavirus testing site" and how the country is effectively using technology to combat the spread of the virus.

However, without policies to safeguard people against a pandemic, containment was initially not possible. A "superspreader" elderly patient (thought to have infected more than a hundred people in her church) was able to refuse testing several times even when suffering all the common symptoms of COVID-19, arguing that she had not travelled overseas and also did not have the money (130 USD) to pay for a detection test. She was let go by authorities twice due to similar reasons as there was no law in place to force anyone to take the test against their wishes. Policies to make the tests free-of-charge for people with symptoms were put in place only after the story was publicized by journalists. Now, anyone can take a test through drive-thru detection stops but must pay a fee of 130 USD if tested negative. By the 8th week from the initial outbreak, South Korea had already tested 307,024 people.

Thanks to the rapid detection employed by the authorities, Korea's mortality rate is low, standing at 2.3% as of April 30th. Such mortality rate figures are a lot lower than developed countries that have gained good publicity for handling the pandemic well, such as Sweden (12.0%) or the Netherlands (11.9%). Rapid detection and contact tracing have also avoided the need to undergo complete nationwide lockdown, and this is despite experiencing peaks with thousands of positive cases a day, thus allowing the economy to perpetually function throughout the pandemic.



All you need is a little push: Sweden's COVID-19 response - *Nordic region*

When COVID-19 arrived in the Northern European hemisphere, most Nordic countries declared internationally that the COVID-19 pandemic would be dealt with swiftly with a complete lockdown of the country's non-essential services to the public. However, Swedish Prime Minister Stefan Lofven took a big gamble to ban foreigner entry and events that gathers more than 50 people, but otherwise all other activities in the country were to resume as normal. Sweden was not armed with a "pandemic disease law" that allowed ministerial powers to be enforced upon the people. Given its unique and urgent circumstances, instead of creating a new law for such powers to be available (the government did so eventually in April), an eloquent speech was given to assure people that the Swedish culture is respected and responsible because just a little "nudge" would do better to encourage social conscience on Swedes than harsh penalties of the law.

Surprisingly, this partially worked. Sweden's medical facilities were so well developed that people needing intensive care were rapidly climbing but never overwhelmed the hospital networks even during its peak infection period in March and April. However, the death toll reached 12% (highest among Nordic countries) as aged citizens in care

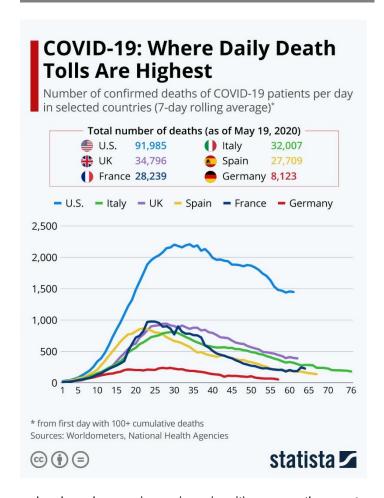
homes were completely devastated by the pandemic. These accounted for more than 60% of all deaths. As of May 12th, Sweden is keeping its policy of "no lockdown" firm and steady, despite repeated warnings from WHO. Sweden went further to argue that people in Sweden's capital of Stockholm already had a 20% infection rate (based on a computer model derived from contact tracing) and it wouldn't be long before Swedish people would reach "herd immunity" and live together with the virus permanently. Ironically, the term "herd immunity" was created to describe the importance of vaccination and not of fatal disease, so this large-scale strategy continues without precedent.

Freedom at a cost: United States' COVID-19 response – *America*

The United States was ranked No. 1 in five of six categories assessed in preparation of a pandemic, according to a John Hopkins study that covered 195 countries back in October 2019. It was the only country that created a "global health unit" structured to be staffed directly by the White House national security staff, and was vital in maintaining leadership capabilities to coordinate a worldwide pandemic response if another Ebola-like outbreak were to ensue. The reporting system created by the White House was well ahead of any other country, except that it was disbanded during downsizing of White House staff in 2018 as "Ebola was largely contained".

To date no organization or unit exists in the world other than the WHO that can coordinate such a gargantuan task, except that it has neither the political power nor the manpower to do anything beyond issuing notices and guidelines for the rest of the world to adhere to voluntarily. New York City is now the epicenter of the global outbreak, accounting for nearly one-third of the worldwide total cumulative positive cases to date. For an outbreak that began and ramped up in the West Coast of the country, the pandemic epicenter eventually switching to the East Coast city of New York is rather astounding. One possible explanation is that West Coast states took the pandemic more seriously. California was one of the first states to declare a statewide lockdown policy to contain the spread of the virus, while New York City (NYC) did not do so until much later, when the case numbers increased well into the exponential phase.

So two facts are evident: there was no coordination of response between states when dealing with the pandemic, and lockdown appears to work in the United States. Interestingly, protests against the lockdown and stay at home



orders have been going on in major cities across the country. Demonstrators are crowding city halls and governmental buildings at the expense of the lockdown, arguing that the people should be best left to decide if they should keep shops open and not one's state or the government. As of this writing, New York is still under a statewide "shelter in place" order. Other than stay at home/lockdown type orders, experts believe contact tracing would help in containing the viral spread, but the administrative burden may be well beyond practice at this point. This is evident by the fact that to diagnose four cases of measles last year, 300 individuals were assessed.

Now that the COVID-19 positive cases have passed one million people, contact tracing may sound unrealistic, yet it is proposed to be the best way to eliminate a second wave of outbreaks in the community. Logically, contact tracing is particularly beneficial after a lockdown, when new cases have tapered to a manageable level for medical

administrators to start the process. Nevertheless, the United States may well be one of the first to provide a solution to this worldwide pandemic: it was one of the first few countries to perform human vaccine trials in March. Many U.S. companies have been swiftly funded by the Department of Defense to generate vaccine candidates against COVID-19, and Wall Street has also supported these same companies by boosting and sustaining a healthy increase in their stock prices. This allows the biotech companies to rapidly expand their vaccine development strategy with newfound abundant financial resources.

Thoughts for the future:

Globally, there has been a lot of debate regarding how one country may have dealt with the COVID-19 crisis better than another, but direct comparisons of numbers and figures between countries largely ignore the political makeup and limitations that the countries' leaders face. Also, every culture has a political incentive to respond in a way that would rally support of its people. But a virus has no political agenda and facing such an efficient and versatile enemy requires a systematic and scientific approach to win. For developed nations, detection, contact tracing and lockdown appear to play important roles in driving effective policy responses to reduce community spread of the virus. More importantly, governing bodies and institutions acting in unison with peoples' trust is a critical component in controlling the severity of infection within a country.

About the Author:



Shin La Shu, PhD is a postdoctoral fellow in the Department of Medicine. He is the co-chair of the Exosome Working Group. He also volunteers as an advisor for Singapore based society, The Society for Hereditary Disorders of Connective Tissue. He is interested in the impact of current affairs on scientific research and development.

EMOTIONAL DISTRESS AMONG HEALTHCARE WORKERS

ASHLEY STENZEL

It's likely as you've scrolled through your social media pages or your news sources, you've seen opinion pieces published by clinicians working in the times of COVID-19. "A New York Doctor's Coronavirus Warning: The Sky Is Falling" a piece in the New York Times is titled. A piece in Politico titled "I'm an ER doc and I'm scared" delivers an equally chilling message. Scrolling through Twitter, the disheartening experiences of healthcare workers fighting the COVID pandemic on the frontlines of New York City, and around the world, are abundant.

In the Politico article, emergency medicine clinician, Sandra Simons, states "Being an ER doctor as our country braces for the impact of COVID-19 feels like standing on the shore and watching a tsunami approach." A video released by the New York Times "People are dying: 72 hours inside a N.Y.C. hospital battling coronavirus" follows Dr. Colleen Smith through an emergency department in Queens, New York. In this video, Dr. Smith shows the emergency department exceeding capacity and a refrigerated truck behind the department to hold the bodies of the deceased. In this video she describes the distress among not only patients, but workers in American hospitals. More recently, an ER physician, Dr. Lorna Breen, who had been working in a Manhattan hospital during COVID-19 committed suicide. Dr. Breen's family described her as not having a history of mental illness but being largely affected by caring for patients during the pandemic. Therefore, it is important to understand the needs of staff who are working during this pandemic.

In an effort to learn more about the support staff may need following COVID-19, we sent questions to current medical providers around the country to hear about their experiences. We learned that many have been informed they should not speak out; however, an internal medicine provider from the Midwest did respond to our request to learn more about what it is like for healthcare workers during this time. They stated "From changing clothes in the garage before and after work, to the mask I put on walking through the door, to lack of



shared environments for our teams, to the best practice advisory pop-up on my pre-rounding chart to screen for COVID, I can't think of an aspect of my work that has not been changed by this event. Quality of life has decreased. I feel trapped. I go to work and get stressed. Then I come home to a newborn. I wash and scrub and try to clean myself, but I feel anxious every time I come home that I may end up giving this virus to my family. Mental health

is on standby. After medical school, I think most of us had to learn to deal with the fatality and the responsibility of the profession for the first time, which was daunting. I felt traumatized. Now is similar, but on a whole new level. While we have much hardship ahead, we need to think about the future after we have survived and navigated through this time. With the way medicine has been practiced and laws changing, the healthcare system and delivery of care has now changed for the future of Americans. We are not limitless in our resources."

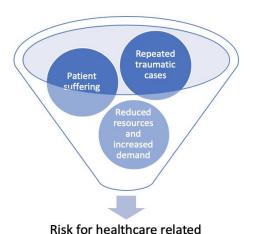
As we meet what is expected to be the peak of our infections and deaths in much of the U.S., it will be important to consider the impact of this pandemic on the mental health and wellbeing of the clinicians, nurses, and many other healthcare workers who sacrifice their own welfare to help others during these times.

Studies have found significantly increased levels of post-traumatic stress disorder (PTSD) among clinicians and nurses caring for patients in a setting where high levels of deaths are observed, particularly among those in the emergency setting, or those handling incidents with mass casualties. One study found that ~16% of emergency room physicians met the criteria for PTSD. Beyond PTSD, there is the concern for compassion fatigue (CF). CF is described as a phenomenon among healthcare workers in which experiences with patients who suffer can lead to feeling burnt out and feeling that it is difficult to cope with the emotions following repeated exposure to such distressing patient outcomes. Some studies have reported a range of 38-60%

SCIENCE IN FOCUS

of clinicians suffering from CF, across different specialties. Following-up with healthcare workers post-pandemic will be a critical step in addressing potential PTSD and CF.

Roswell Park has released a webinar regarding mental health during the pandemic (found here: https://www.youtube.com/watch?v=oQj0xxKqDll&feature=e mb logo), has created staff "sanctuaries" for employees working on campus during these stressful times, and also has resources available on i2 for Roswell employees. Continued conversations as to how we can best support healthcare workers dealing with the aftermath of the pandemic will be necessary.



PTSD or CF

If you or somebody you know is struggling, please seek out resources for help including the NYS crisis prevention line: 1-800-273-8255

Also available for Roswell employees are Roswell Park mental health resources: https://i2proxy.roswellpark.org/pages/read/e4db937c-077d-4526-933c-daf1f4123732

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Ashley Stenzel is a doctoral candidate in the department of cancer prevention and control in the lab of Kirsten Moysich, PhD. Ashley has a background in clinical research, scientific affairs, and currently is exploring disparities and immunosuppression in ovarian cancer patients. In addition, she is the co-founder for the Buffalo pod of 500 Women Scientists.



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